REMARKS

I. Disposition of the Claims

Claims 1-40 and 44-47 are pending. Claims 1-40 are subject to a restriction requirement. Claims 41-43 have been cancelled without prejudice or disclaimer. Claims 44-47 are new and should be grouped in group I. Claims 1-2, 4-12, 14-22, 24-32, and 34-40 have been rejected under 35 USC § 112, second paragraph. Claims 11, 14, and 31 have been rejected under 35 USC § 102. Claims 3, 13, 23, and 33 have been objected to for depending on a rejected base claim but are otherwise allowable if rewritten in independent form. Office action, p. 5.

Claims 1, 4, and 7 have been amended to correct an inadvertent typographical error. Claim 10 has been amended to change its dependency. Claims 11 and 14 have been amended to narrow the choice of R_3 substituents. Claims 44-47 are new and supported in the as-filed specification, e.g., claims 1, 11, 21, and 31; pp. 81-et seq. Thus, written description support is in the specification as-filed.

The term "C_1-C_9 alkyl" should be interpreted to include both straight and branched alkyls.

The PTO is thanked for indicating allowable subject matter. Office action, para. 4.

II. Objection to the Specification

The specification has been objected to because "''pyrazinecarboxylate' ... is inconsistent with the formula when n equals 1." Office action, p. 2. This amendement adds the text of claims 3 and 13 in the appropriate location of the specification. No new matter has been added. Thus, this objection should be withdrawn.

III. Rejections under 35 USC § 112, second paragraph

Claims 1-2, 4-12, 14-22, 24-32, and 34-43 have been rejected as indefinite for five reasons, each of which are addressed under a separate subsection enumerated as in the Office action. Office action, p. 3. Claims 41-43 have been canceled.

a. Claims 1, 4, 7, 11, 14, 17, 21, 24, 27, 31, 34, and 37 have been rejected for using the term "*heterocycle is unsubstituted **on** substituted*." Office action, p. 3. Claims 1, 4, and 7 have been amended to correct the inadvertent typographical error. Claims 11, 14, 17, 21, 24, 27, 31, 34, and 37 never raised this issue. See p. 119, l. 3; p. 122, l. 3; p. 125, l. 3; p. 128, l. 1; p. 131, l. 1; p. 134, l. 1; p. 136, l. 6; p. 139, l. 6; and p. 142, l. 6. The analogous term in the present version of these claims lacks the inadvertent typographical error, i.e., the word --or--, not "on," is in this term. Thus, the rejection should be withdrawn.

b. Claims 1, 4, 7, 11, 14, 17, 21, 24, 27, 31, 34, and 37 have been rejected for using, in R_1's definition, the terms "COOH," "$COOR_3$," and "COR_3," which have "double inclusions when R_3 is hydrogen [or] hydroxy...." Office action, p. 3. Yet just because a compound may be embraced by more than one member of a Markush group of a claim does not lead to any uncertainty as to the scope of that claim. MPEP § 2173.05(o). "For example, the Markush group, 'selected from the group consisting of amino, halogen, nitro, chloro and alkyl' should be acceptable even though 'halogen' is generic to 'chloro.'" MPEP § 2173.05(h). Similarly, in this rejection the cited terms should be acceptable even if $COOR_3$ and COR_3 are generic to COOH.

The proper test is whether the claim reasonably apprises one of ordinary skill in the art of its scope. MPEP § 2173.02. And since the rejection identifies various ways to construct a particular group (COOH) from cited terms, the cited terms should reasonably apprise one of ordinary skill in the art of its scope. Thus, this rejection is improper and should be withdrawn.

c. Claims 2, 5-6, 8-10, 12, 15-16, 18-20, 22, 25-26, 28-30, 32, 35-36, and 38-40 have been rejected as depending on a rejected claim. Office action, p. 3. It is respectfully submitted that each of these claims avoids this issue. Thus, this rejection is improper and should be withdrawn.

d. Claim 41 has been rejected as indefinite for reciting two different variable Xs. Office action, p. 3. Claim 41 has been cancelled. Thus, this rejection should be withdrawn.

e. Claims 41-43 have been rejected for being indefinite, because "it is unclear how the other functional groups defined by R_1 can be prepared from said starting materials." Office action, pp. 3-4. Claims 41-43 have been cancelled. Thus, this rejection should be withdrawn.

IV. Rejections under 35 USC § 102

Various claims have been rejected as anticipated by the disclosures of Kobayashi (EP 0 104,484) and Delaszlo (US Pat. No. 6,069,163). Each rejection is addressed under a separate subheading.

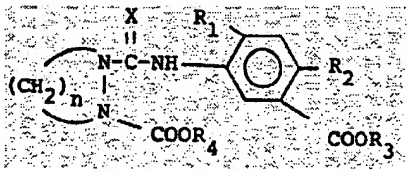
A. Kobayashi

Absent a description of all limitations, a document neither describes nor anticipates the claim. MPEP § 2131. Such is the case in this rejection, where Kobayashi never describes or anticipates a compound of claim 31, which was rejected as anticipated by Kobayashi's compounds 39-41. Office action, p. 4.

Kobayashi contains the following cited disclosure:

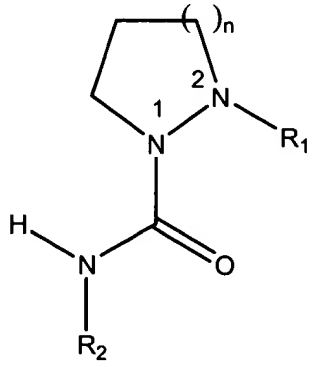
Tabl 2

Compound No.	n	X	R_1	R_2	R_3	R_4
39	3	O	F	Cl	CH_3	C_2H_5
40	3	O	F	Cl	C_2H_5	"
41	3	O	F	Cl	C_3H_7(i)	"



Kobayashi, pp. 17-18. Note particularly that the aromatic $-COOR_3$ group (lower-right-hand side) is an ester, since R_3 is CH_3, C_2H_5, or C_3H_7 (i).

On the other hand, claim 31 recites a compound of formula IV:



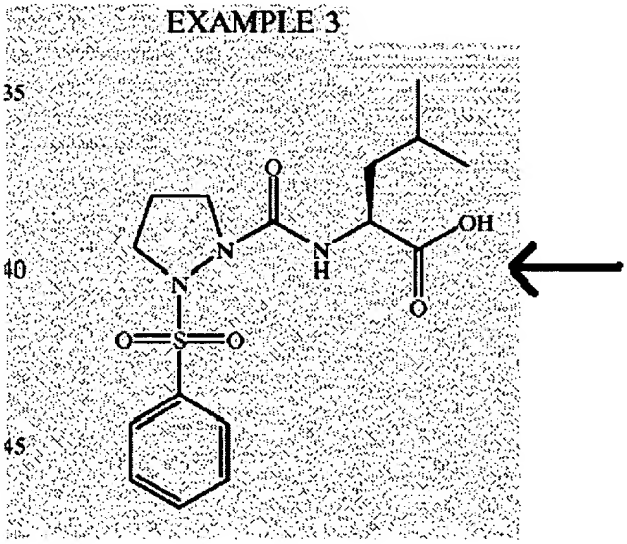
IV

in which R_2 may be an aryl substituted with one or more substituents selected from those other than Kobayashi's ester groups.

As a result, since the presently claimed R_2-aryl substitutents cannot be selected from Kobayashi's ester groups, and since the Kobayashi's cited-aromatic $-COOR_3$ groups are particular esters, the presently claimed compounds differ from those of Kobayashi. In other words, Kobayashi neither describes nor anticipates the compound of claim 31. Thus, this rejection is improper and should be withdrawn.

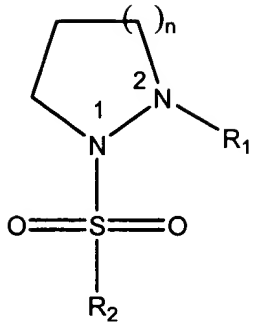
B. Delaszlo

Claims 11 and 14 stand rejected as anticipated by Delaszlo's compound 3:



Office action, p. 5. Note particularly compound 3's acid group in the structure's upper-right-hand side.

The present versions of claims 11 and 14 avoid this issue. Specifically, claims 11 and 14 recite a compound of formula II:



II

in which R_1 may be -CON(R_3)$_2$, and R_3 may be C_1-C_9 alkyl optionally substituted with substituents other than carboxy (COOH).

As neither claim 11 nor 14 embraces Delaszlo's compound 3, Delaszlo neither describes nor anticipates claim 11 or 14. Thus, this rejection is improper and should be withdrawn.

CONCLUSION

Applicant respectfully requests reconsideration and reexamination of the present application. Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

Date 1/24/03

By _____

FOLEY & LARDNER
Customer Number: 29728
29728
PATENT TRADEMARK OFFICE
Telephone: (202) 295-4166
Facsimile: (202) 672-5399

Sean A. Passino
Attorney for Applicant
Registration No. 45,943

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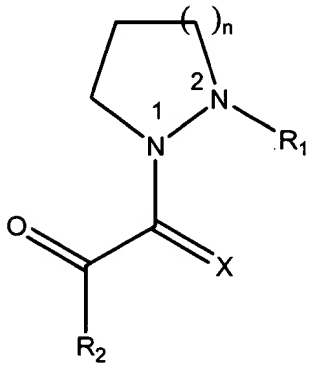
In the Claims:

1. (Amended) A compound of formula I

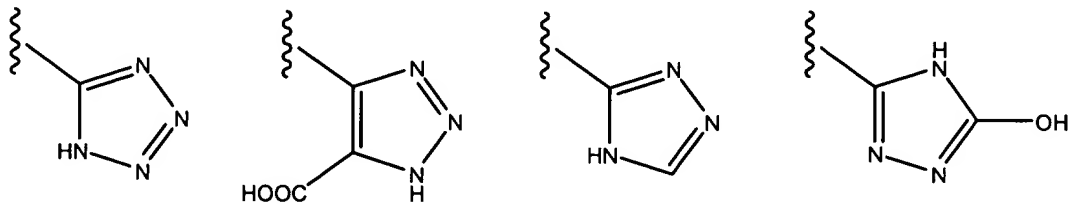


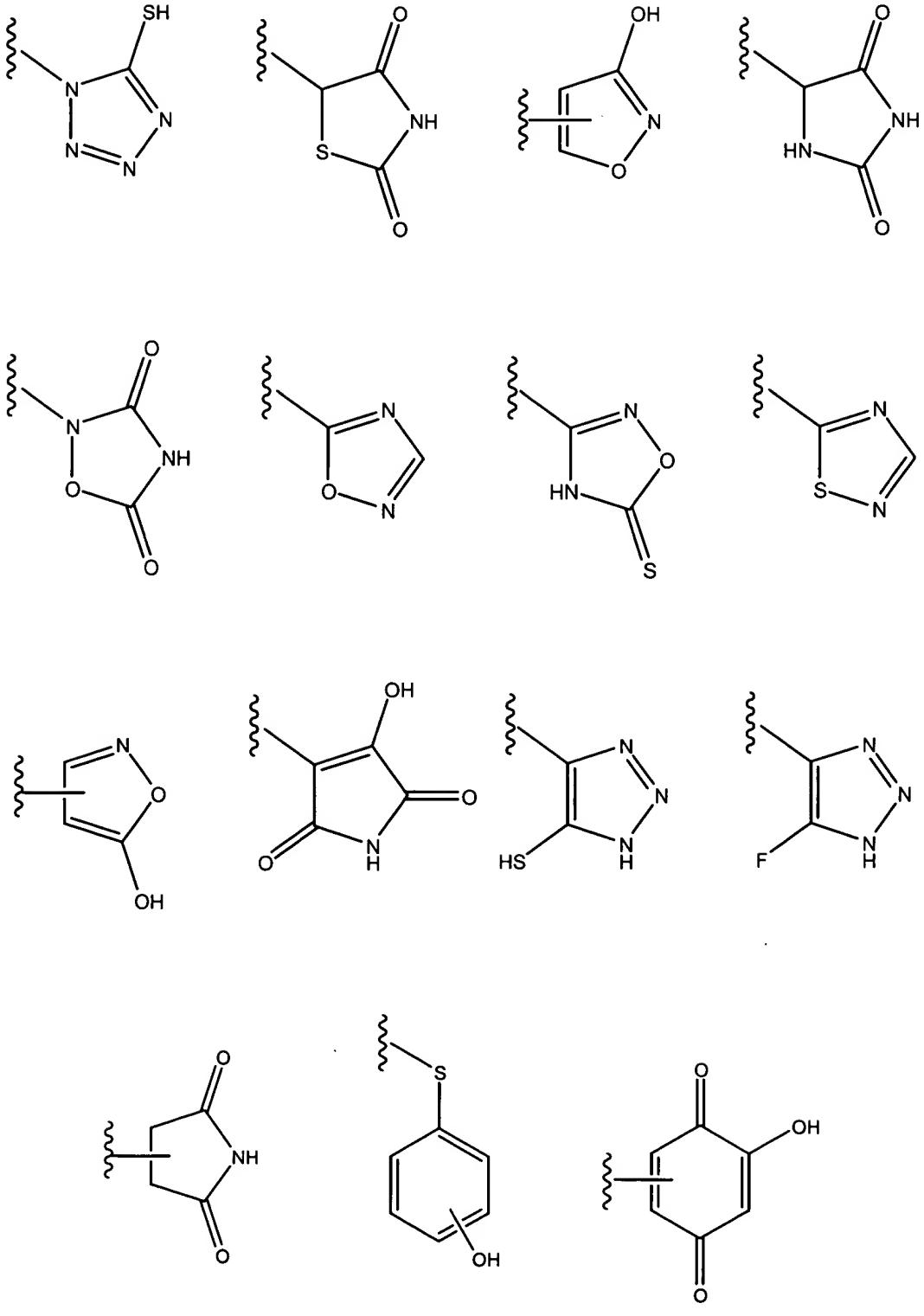
I

or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

n = 1-3;

R_1 is selected from the group consisting of $-CR_3$, $-COOR_3$, $-COR_3$, -COOH, $-SO_3H$, $-SO_2HNR_3$, $-PO_2(R_3)_2$, -CN, $-PO_3(R_3)_2$, $-OR_3$, $-SR_3$, $-NHCOR_3$, $-N(R_3)_2$, $-CON(R_3)_2$, $-CONH(O)R_3$, $-CONHNHSO_2R_3$, $-COHNSO_2R_3$, $-CONR_3CN$,





wherein said R_1 group is either unsubstituted or additionally substituted with R_3;

R_2 is selected from the group consisting of hydrogen, C_1-C_9 straight or branched chain alkyl, C_2-C_9 straight or branched chain alkenyl, C_2-C_9 straight or branched chain alkynyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted [on] or substituted with one or more substituents selected from R_3;

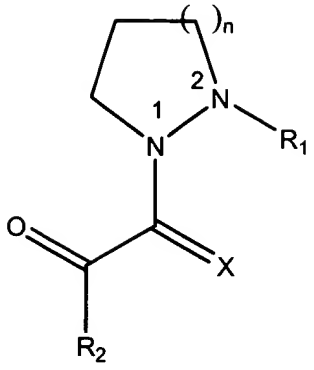
R_3 is selected from the group consisting of hydrogen, C_1-C_9 alkyl, C_2-C_9 straight or branched chain alkenyl, C_2-C_9 straight or branched chain alkynyl, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C_1-C_9 thioalkyl, C_2-C_9 thioalkenyl, C_1-C_9 alkylamino, C_2-C_9 alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocyle, or heterocycle group; and

X is O or S.

4. (Amended) A pharmaceutical composition comprising:

(i) a therapeutically effective amount of a compound of formula I:

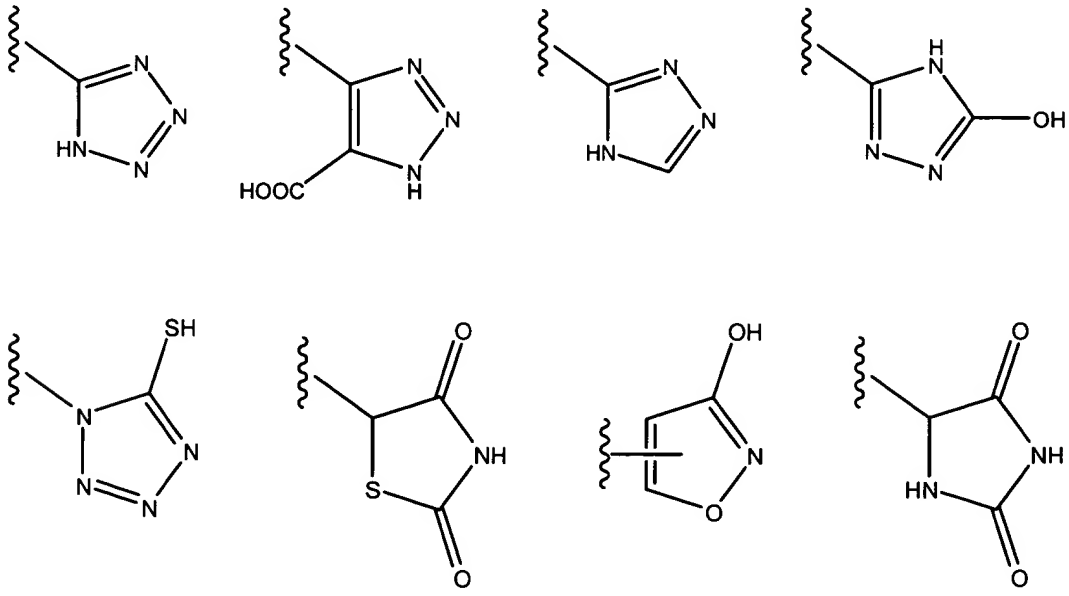


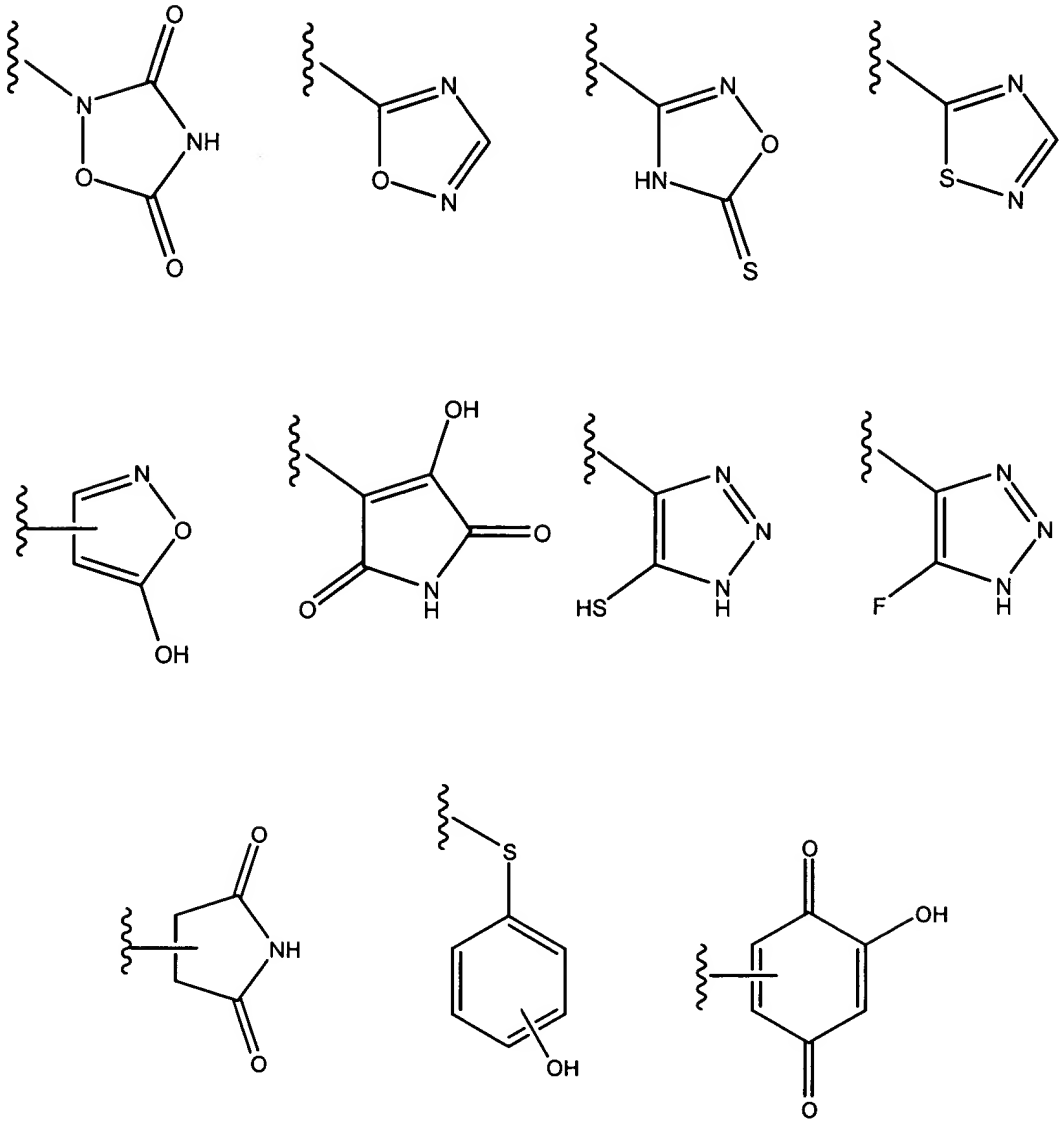
I

or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

n = 1-3;

R_1 is selected from the group consisting of $-CR_3$, $-COOR_3$, $-COR_3$, -COOH, $-SO_3H$, $-SO_2HNR_3$, $-PO_2(R_3)_2$, -CN, $-PO_3(R_3)_2$, $-OR_3$, $-SR_3$, $-NHCOR_3$, $-N(R_3)_2$, $-CON(R_3)_2$, $-CONH(O)R_3$, $-CONHNHSO_2R_3$, $-COHNSO_2R_3$, $-CONR_3CN$,





wherein said R_1 group is either unsubstituted or additionally substituted with R_3;

R_2 is selected from the group consisting of hydrogen, C_1-C_9 straight or branched chain alkyl, C_2-C_9 straight or branched chain alkenyl, C_2-C_9 straight or branched chain alkynyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, alkynyl,

aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted [on] or substituted with one or more substituents selected from R_3;

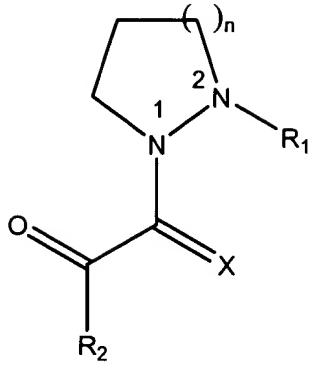
R_3 is selected from the group consisting of hydrogen, C_1-C_9 alkyl, C_2-C_9 straight or branched chain alkenyl, C_2-C_9 straight or branched chain alkynyl, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C_1-C_9 thioalkyl, C_2-C_9 thioalkenyl, C_1-C_9 alkylamino, C_2-C_9 alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocyle, or heterocycle group; and

X is O or S; and

(ii) a pharmaceutically acceptable carrier.

7. (Amended) A method for affecting a neuronal activity in a mammal, comprising administering to the mammal an effective amount of a compound of formula I:

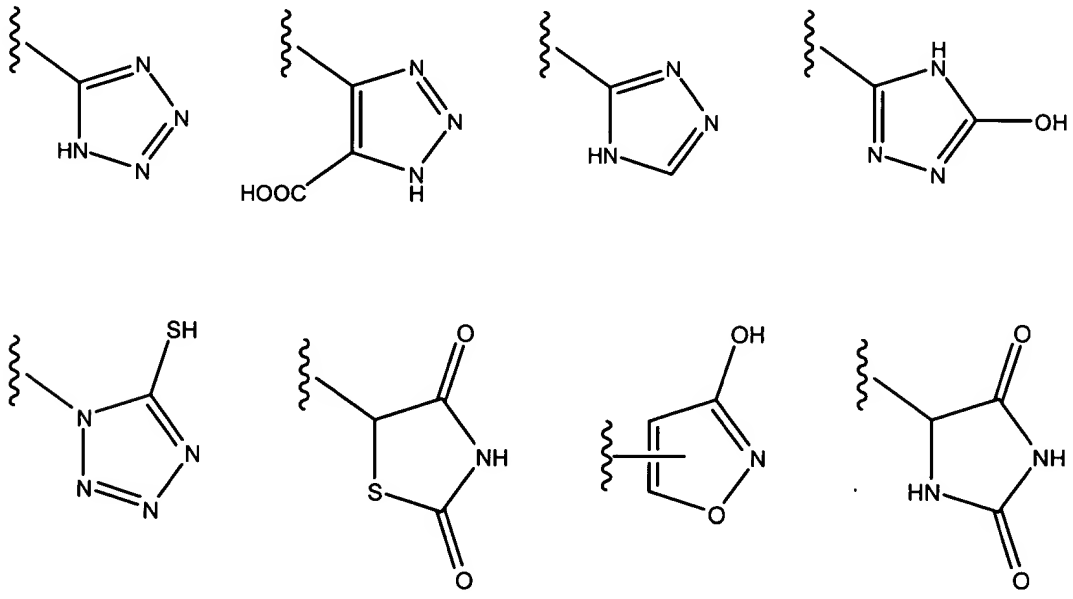


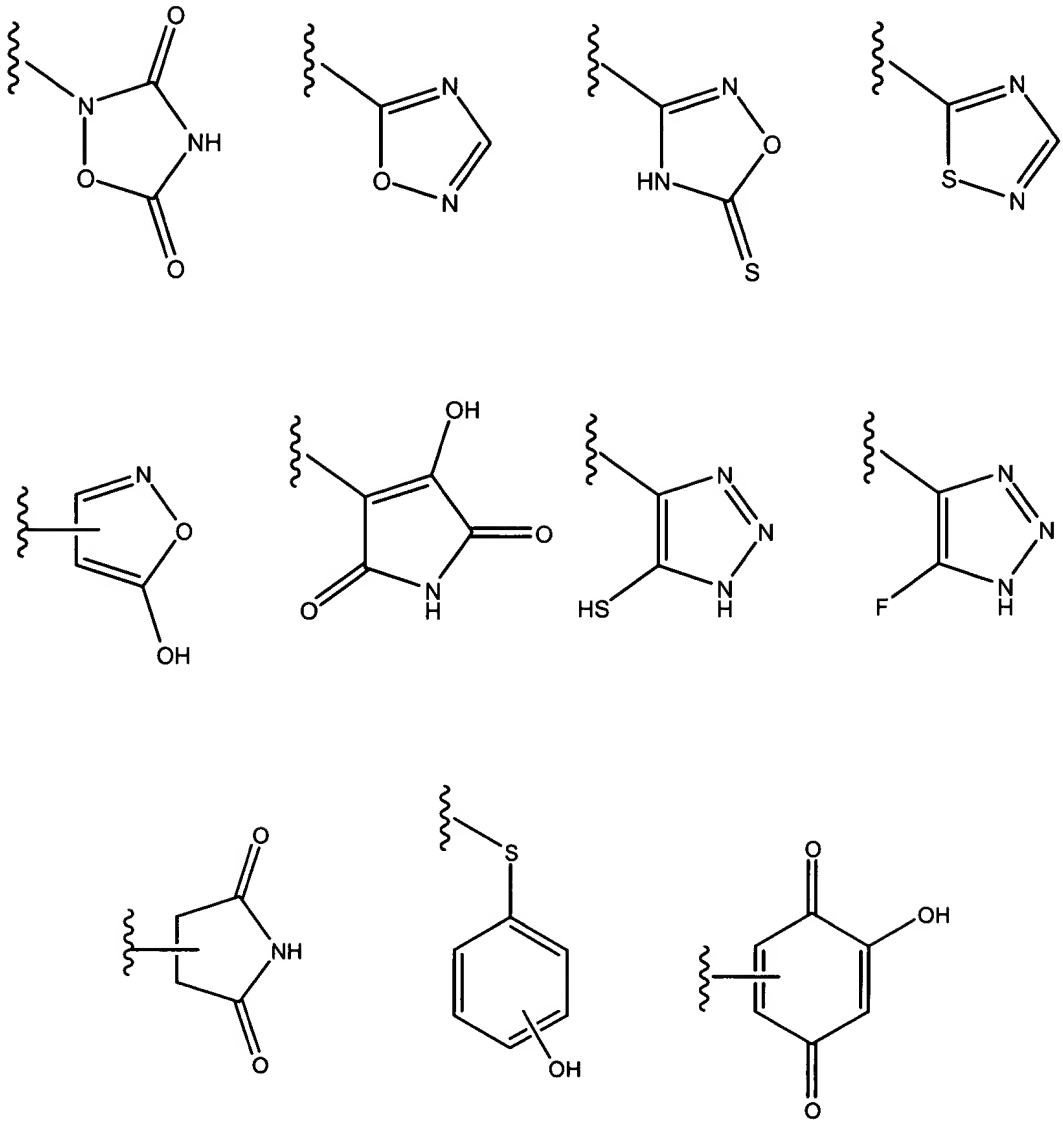
I

or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

n = 1-3;

R_1 is selected from the group consisting of $-CR_3$, $-COOR_3$, $-COR_3$, -COOH, $-SO_3H$, $-SO_2HNR_3$, $-PO_2(R_3)_2$, -CN, $-PO_3(R_3)_2$, $-OR_3$, $-SR_3$, $-NHCOR_3$, $-N(R_3)_2$, $-CON(R_3)_2$, $-CONH(O)R_3$, $-CONHNHSO_2R_3$, $-COHNSO_2R_3$, $-CONR_3CN$,





wherein said R_1 group is either unsubstituted or additionally substituted with R_3;

R_2 is selected from the group consisting of hydrogen, C_1-C_9 straight or branched chain alkyl, C_2-C_9 straight or branched chain alkenyl, C_2-C_9 straight or branched chain alkynyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, alkynyl,

aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted [on] or substituted with one or more substituents selected from R_3;

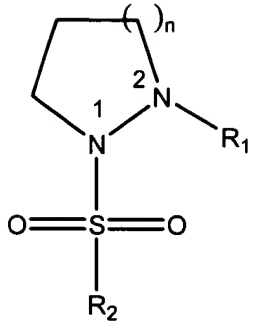
R_3 is selected from the group consisting of hydrogen, C_1-C_9 alkyl, C_2-C_9 straight or branched chain alkenyl, C_2-C_9 straight or branched chain alkynyl, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C_1-C_9 thioalkyl, C_2-C_9 thioalkenyl, C_1-C_9 alkylamino, C_2-C_9 alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocyle, or heterocycle group; and

X is O or S.

10. (Amended) The method of claim [11] 9, wherein the neurological disorder relating to neurodegeneration is selected from the group consisting of Alzheimer's disease, Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis.

11. (Amended) A compound of formula II:

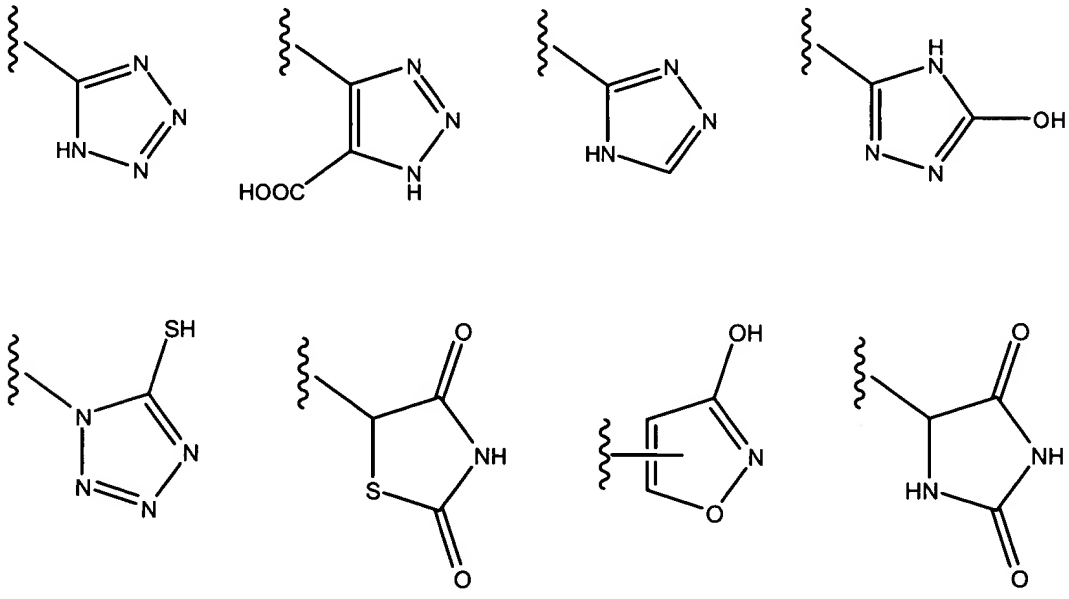


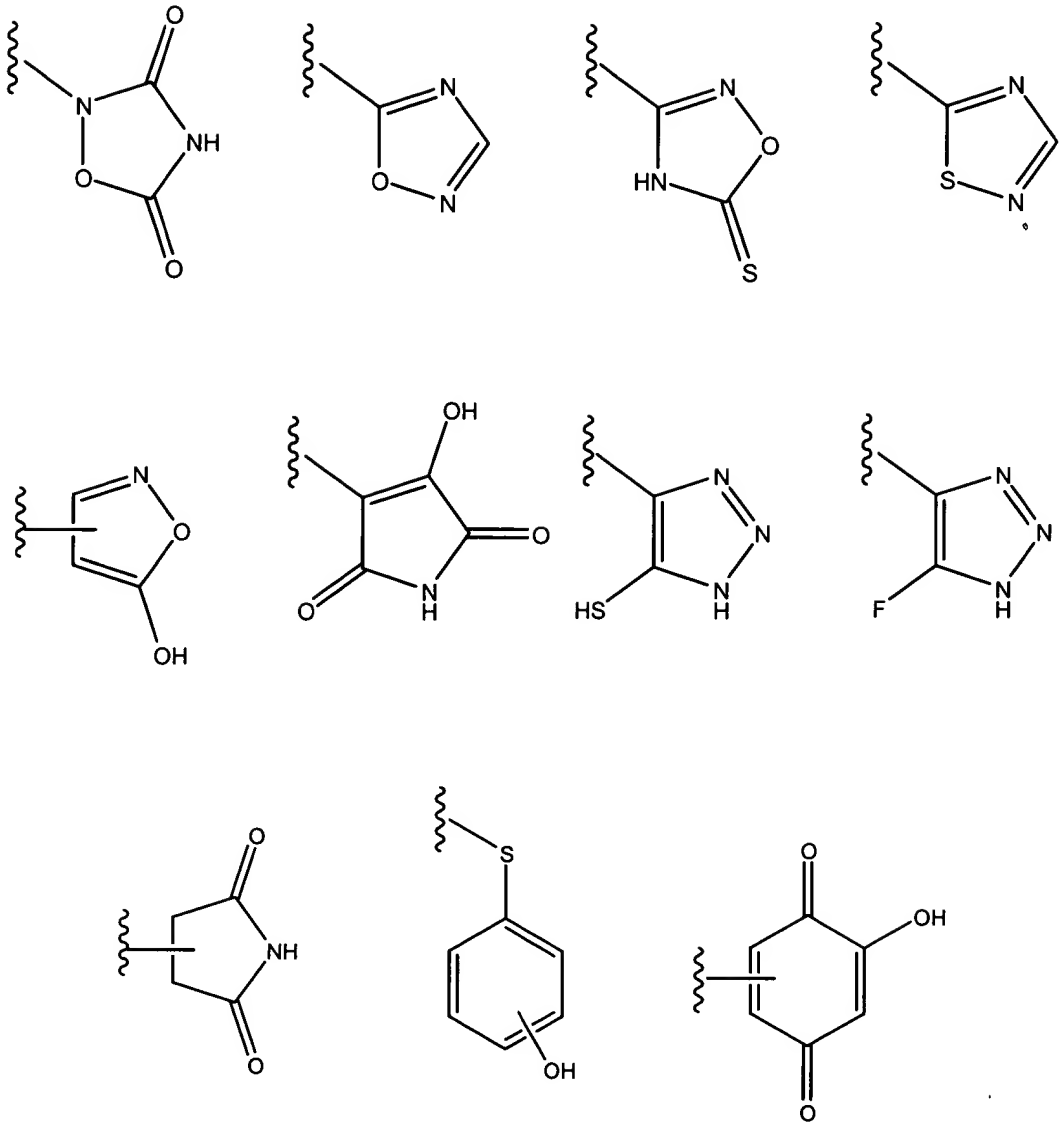
II

or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

n = 1-3;

R_1 is selected from the group consisting of $-CR_3$, $-COOR_3$, $-COR_3$, -COOH, $-SO_3H$, $-SO_2HNR_3$, $-PO_2(R_3)_2$, -CN, $-PO_3(R_3)_2$, $-OR_3$, $-SR_3$, $-NHCOR_3$, $-N(R_3)_2$, $-CON(R_3)_2$, $-CONH(O)R_3$, $-CONHNHSO_2R_3$, $-COHNSO_2R_3$, $-CONR_3CN$,





wherein said R_1 group is either unsubstituted or additionally substituted with R_3;

R_2 is selected from the group consisting of hydrogen, C_1-C_9 straight or branched chain alkyl, C_2-C_9 straight or branched chain alkenyl, C_2-C_9 straight or branched chain alkynyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, alkynyl,

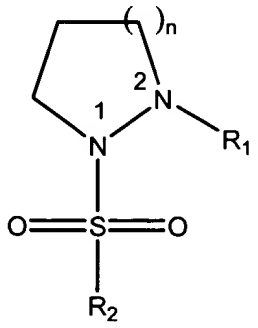
aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted or substituted with one or more substituents selected from R_3;

R_3 is selected from the group consisting of hydrogen, C_1-C_9 alkyl, C_2-C_9 straight or branched chain alkenyl, C_2-C_9 straight or branched chain alkynyl, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, **[carboxy,]** C_1-C_9 thioalkyl, C_2-C_9 thioalkenyl, C_1-C_9 alkylamino, C_2-C_9 alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocyle, or heterocycle group.

14. (Amended) A pharmaceutical composition comprising:

(i) a therapeutically effective amount of a compound of formula II:

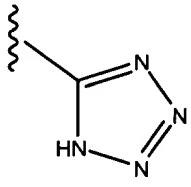
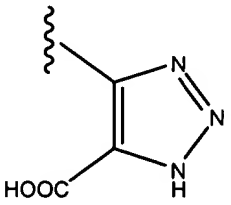
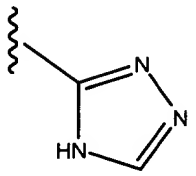
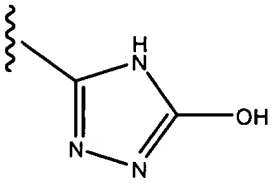
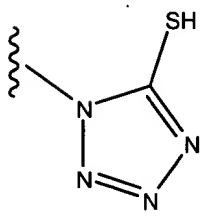
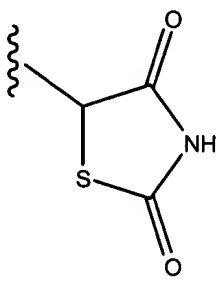
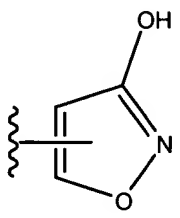
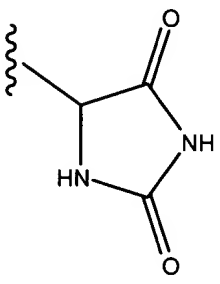
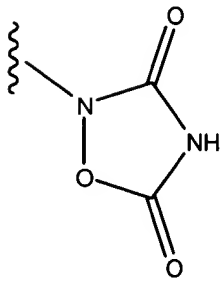
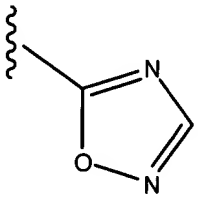
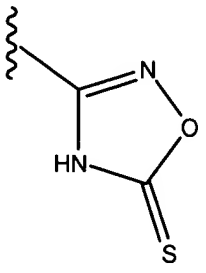
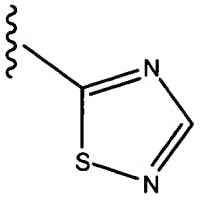


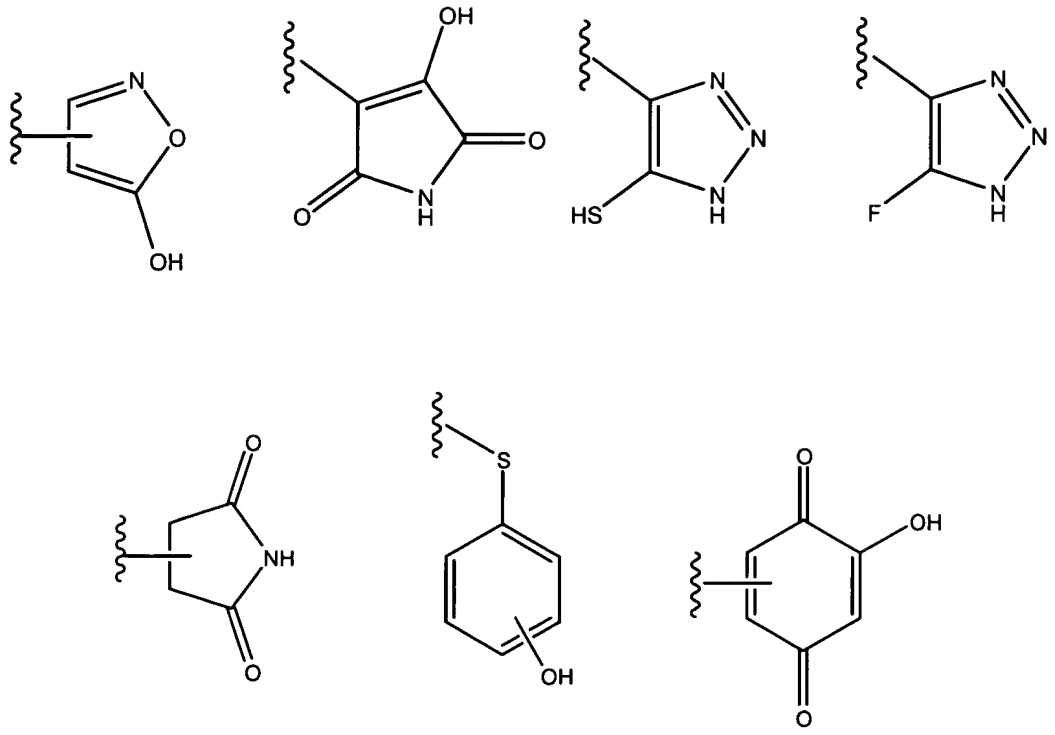
II

or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

n = 1-3;

R_1 is selected from the group consisting of $-CR_3$, $-COOR_3$, $-COR_3$, -COOH, $-SO_3H$, $-SO_2HNR_3$, $-PO_2(R_3)_2$, -CN, $-PO_3(R_3)_2$, $-OR_3$, $-SR_3$, $-NHCOR_3$, $-N(R_3)_2$, $-CON(R_3)_2$, $-CONH(O)R_3$, $-CONHNHSO_2R_3$, $-COHNSO_2R_3$, $-CONR_3CN$,



wherein said R_1 group is either unsubstituted or additionally substituted with R_3;

R_2 is selected from the group consisting of hydrogen, C_1-C_9 straight or branched chain alkyl, C_2-C_9 straight or branched chain alkenyl, C_2-C_9 straight or branched chain alkynyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted or substituted with one or more substituents selected from R_3;

R_3 is selected from the group consisting of hydrogen, C_1-C_9 alkyl, C_2-C_9 straight or branched chain alkenyl, C_2-C_9 straight or branched chain alkynyl, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, **[carboxy,]** C_1-C_9 thioalkyl, C_2-C_9 thioalkenyl, C_1-C_9 alkylamino, C_2-C_9 alkenylamino, cyano, nitro, imino, sulfonyl,

thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, carboxy, carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocyle, or heterocycle group; and

(ii) a pharmaceutically acceptable carrier.